REMARKS

Claims 8-31 and 43-45 are presently pending. Of these, Claims 10-15, 17-21, 24-30 are withdrawn from consideration. Support for amendments to Claim 8 is found in the specification as filed, for example at page 15, lines 18-22, and Example 5 given at page 27, line 15 through page 28, line 26. No new matter has been added herewith. The following addresses the substance of the Office Action.

Indefiniteness

Claim 9 was rejected under 35 U.S.C. § 112, second paragraph as being indefinite. In particular, the claim recited properties of a product, but required an active step. Thus, it was unclear if the claimed invention is a product or a method. Applicant has amended Claim 9 by deleting language pertaining to an active step. Specifically, recitation of "for intestinal delivery of the therapeutic agent, and administering is by oral administration" was deleted. In view of the amendment, the Applicant respectfully requests that the rejection be withdrawn.

Anticipation

Claims 8, 9, 16 and 43 were rejected under 35 U.S.C. § 102(b) as being anticipated by Potter et al. (U.S. Patent No. 5,422,110). Potter et al. discloses fusion proteins based on the bacterial protein leukotoxin and selected antigens, including VP4. The only "VP4" embodiment disclosed by the reference is described in Example 2 and is depicted in Figures 9 and 10. Referring to Figure 10, particularly at Figure 10-10, the fusion protein consists of recombinant leukotoxin peptide and a 15 amino acid peptide that corresponds to amino acids 240-255 of the Rhesus Monkey VP4 protein sequence provided by SEQ ID NO: 1 of the present application.

To clearly distinguish over the cited reference, the Applicant has amended the claims to be limited to a pharmaceutical composition for the delivery of a therapeutic agent comprising: (A) a therapeutic agent; and (B) an effective amount of a protein or peptide related to VP8 protein.

To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed.Cir. 1986). "[A]nticipation requires that all of the elements and limitations of the claim are found within a single prior art reference." *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991). The VP8 protein (SEQ ID NO: 2) comprises

the first 231 amino acids of VP4 (SEQ ID NO: 1). In contrast, Potter et al. refers to a chimeric protein consisting of VP4 or a peptide taken from a position that corresponds to amino acids 240-255 of the Rhesus Monkey VP4 protein, which is downstream of the VP8 sequence. In view of the amendment to Claim 8, the claims are not anticipated by Potter et al. and the Applicant respectfully requests that the rejection be withdrawn.

Obviousness

Claims 8, 9, 16, 22, 23, 31 and 43 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Langridge and Arakawa (U.S. Publication No. 2002/0055618 A1), Potter et al. (*supra*) and Honeyman et al. (2000 *Diabetes* **49**:1319-1324). Langridge and Arakawa teach the formation of various fusion proteins, which may contain different autoimmune autoantigens or pathogen autoantigens, such as VP4. The teachings of Potter et al. are discussed above. Honeyman et al. teaches that, in some instances, children infected by rotavirus can develop type 1 diabetes. The Examiner stated that it would have been obvious to one of ordinary skill in the art to modify the compositions taught by Langridge and Arakawa in order to use rotavirus VP4 and insulin in a fusion structure for oral administrations.

As indicated above, the Applicant has amended the claims to be limited to a pharmaceutical composition for the delivery of a therapeutic agent comprising: (A) a therapeutic agent; and (B) an effective amount of a protein or peptide related to VP8 protein. None of the cited references, either individually or in combination, would have given any reason to one of ordinary skill in the art to develop such a composition that specifically contains the VP8 protein or a peptide derived from VP8.

Referring to Examples 1-6 of the present specification, the Applicant has discovered that rotavirus VP8 protein and peptides derived from VP8 protein modulate tissue permeability, thereby enhancing passage of the therapeutic agent. The inventors identified domains present in VP8 that resemble the extracellular loops of the tight junction (TJ) proteins occludin and claudin. The inventors discovered that the VP8 protein and peptides derived from VP8 that bear a $\geq$50% similarity to the extracellular loops of claudin and occludin significantly reduce the transepithelial electrical resistance (TER) of Madin-Darby Canine Kidney (MDCK) cells. Based on the prior art of record, there was no reason or suggestion for the skilled artisan to believe that the presently

claimed pharmaceutical compositions would be able to enhance passage of a therapeutic agent through epithelia and endothelia.

In contrast to the presently claimed compositions, Potter et al. teach chimeric proteins, wherein a leukotoxin portion functions to increase the immunogenicity of antigen fused thereto. Similarly, Langridge et al. teach fusion proteins that contain different autoimmune autoantigens or pathogen autoantigens such as VP4. However, nothing in Potter et al. or Langridge et al. would have led the skilled artisan to combine a therapeutic agent, such as insulin, with an effective amount of VP8 or a related VP8 peptide to enhance passage of the therapeutic agent through epithelia and endothelia. The Examiner noted that Honeyman et al. teaches an association between rotavirus infection and pancreatic islet autoimmunity in children at risk of developing Type 1 Diabetes. However, such knowledge would not motivate one of skill in the art to combine a rotavirus protein such as VP4 with a therapeutic agent such as insulin. Instead, the skilled artisan would avoid treating a diabetic patient or any patient with a composition containing a rotavirus protein, which might exacerbate or induce Type 1 Diabetes.

In view of the amendments to the claims and the preceding remarks, the presently claimed compositions are not obvious in view of the cited references and the Applicant respectfully requests that the rejection under 35 U.S.C. § 103(a) be withdrawn.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

In view of Applicants' amendments to the Claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: June 14, 2010

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